REMARKS

The Present Invention

The present invention is directed to a chimeric pIX protein having at least one adenoviral pIX domain and a non-native amino acid sequence. The non-native amino acid sequence encodes a ligand that binds to a substrate present on the surface of a cell. Alternatively, the non-native amino acid sequence encodes an antigen, and the non-native amino acid sequence constitutes the C-terminus of the chimeric pIX protein or is located internally within the chimeric pIX protein. An adenoviral capsid containing a chimeric pIX protein having at least one adenoviral pIX domain and a non-native amino acid sequence also is provided, as well as a composition comprising the adenoviral capsid, an adenoviral vector comprising the adenoviral capsid, and a method of infecting a cell.

The Amendments to the Claims

Claims 1, 4, 5, and 19 have been amended to point out more particularly and claim more distinctly the present invention. Claim 1 has been amended to incorporate the subject matter of originally filed claims 2 and 3, which have been cancelled. The amendment to claim 1 is supported by the specification at, for example, paragraphs 0010 through 0013. Claims 4 and 5 have been amended to correct the dependencies of those claims. Claim 4 also had been amended to recite CD40 protein as supported by the specification at, for example, paragraph 0015. Claim 19 has been amended to place it in independent form by incorporating the subject matter of originally filed claim 1. Claims 41-48 are new. Claim 41 is supported by the specification at, for example, paragraphs 0009 and 0010. Claims 42-48 mirror claims 11-15, 17, and 18, respectively. No new matter has been added by way of these claim amendments and additions. Separate documents setting forth the precise changes to the claims, as well as the text of the pending claims, are attached.

The Pending Claims

Claims 1 and 4-48 are currently pending and are directed to the chimeric pIX protein (claims 1, 4-17, and 41-47), the nucleic acid encoding the chimeric pIX protein (claims 18 and 48), the adenoviral capsid (claims 19-28), the composition comprising the adenoviral capsid (claims 29 and 30), the adenoviral vector comprising the adenoviral capsid (claims 31-38), and the method of infecting a cell (claims 39 and 40).

The Office Action

Claims 1-2, 9, 11, 12, 17, and 18 are rejected under 35 U.S.C. § 102(b), as allegedly being anticipated by Lutz et al. (*J. Virol.*, *71*(7), 5102-5109 (1997)). Claims 1-3, 5, 18, 19,

29-32, and 34-40 are rejected under 35 U.S.C. § 102(a), as allegedly being anticipated by WO 99/36545 (Romanczuk et al.). Reconsideration of these rejections is requested.

Discussion of Rejection under 35 U.S.C. § 102(b)

Claims 1-2, 9, 11, 12, 17, and 18 are rejected under 35 U.S.C. § 102(b), as allegedly being anticipated by Lutz et al. Claim 2 has been cancelled. This rejection is traversed for the reasons set forth below.

Claim 1, as amended, incorporates the features of claim 3 (which was not subject to this rejection). Claim 1, therefore, is directed to a chimeric pIX protein having at least one adenoviral pIX domain and a non-native amino acid sequence encoding a ligand that binds to a substrate present on the surface of a cell. Lutz et al. discloses a fusion protein comprising an amino acid sequence encoding a pIX protein or fragments thereof and an amino acid sequence encoding glutathione s-transferase (GST) or the F domain of the human estrogen receptor (hER). Neither GST nor the F domain of the hER is a ligand that binds to a substrate present on the surface of a cell. Indeed, the non-native amino acid sequences of Lutz et al. merely serve as a means of detection or purification. As such, the disclosure of Lutz et al. does not teach each and every feature of claim 1, and the Section 102(b) rejection of claim 1, as well as claims 9, 11, 12, 17, and 18 dependent thereon, should be withdrawn.

Discussion of Rejection under 35 U.S.C. § 102(a)

Claims 1-3, 5, 18, 19, 29-32, and 34-40 are rejected under 35 U.S.C. § 102(a), as allegedly being anticipated by WO 99/36545. Claims 2 and 3 have been cancelled. This rejection is traversed for the reasons set forth below.

The '545 PCT application discloses the manipulation of adenoviral coat proteins by the insertion of a ligand that binds a cellular receptor. Protein IX is mentioned as an adenoviral coat protein, although no guidance is provided in the '545 PCT application as to how or where to insert a ligand into pIX to generate a functional adenoviral coat protein that binds a cellular receptor. Applicants submit herewith a Declaration under 37 C.F.R. § 1.131, which establishes a date of conception and a date of reduction to practice which predate the publication date of the '545 PCT application. As set forth in the Rule 132 Declaration, Applicants generated a nucleic acid encoding a chimeric pIX protein comprising a non-native amino acid sequence encoding a ligand (such as that encompassed by, for example, pending claim 18) before the publication date of the '545 PCT application. Expression of the nucleic acid sequence yields the chimeric pIX protein of the present invention (see, e.g., claim 1). Incorporation of the nucleic acid sequence into an adenoviral genome and expression thereof yields an adenoviral capsid as claimed in, for example, claim 19. As such, WO 99/36545 is

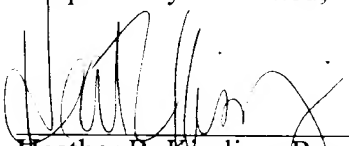
not prior art under Section 102(a) to at least claims 1, 18, and 19, and all claims dependent thereon.

Furthermore, the '545 PCT application does not anticipate the subject matter of new claim 41 or claims dependent thereon. The disclosure of the '545 PCT application is limited to ligands that bind cellular receptors. There is no teaching or suggestion of a chimeric pIX protein having at least one adenoviral pIX domain and a non-native amino acid sequence encoding an antigen. Moreover, there is no teaching or suggestion in the reference where to position the non-native amino acid sequence, e.g., the C-terminus of the chimeric pIX protein or located internally within the chimeric pIX protein, as recited in claim 41. Thus, the cited reference does not teach or suggest each and every feature of claims 41-48 and, therefore, cannot be considered as anticipating those claims, or even rendering obvious the subject matter of those claims.

Conclusion

The application is considered in good and proper form for allowance, and the Examiner is respectfully requested to pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned agent.

Respectfully submitted,



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CERTIFICATE OF MAILING

I hereby certify that this RESPONSE TO OFFICE ACTION (along with any documents referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, Washington, D.C. 20231.

Date: _____ _____

PATENT
Attorney Docket No. 208859

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Roelvink et al.

Art Unit: 1636

Application No. 09/780,224

Examiner: Guzo, D.

Filed: February 9, 2001

For: ADENOVIRAL CAPSIDS CONTAINING CHIMERIC PROTEIN IX

AMENDMENTS TO CLAIMS MADE IN RESPONSE TO OFFICE ACTION DATED JANUARY 3, 2002

Amendments to existing claims:

1. (Amended) A chimeric pIX protein having at least one adenoviral pIX domain and a non-native amino acid sequence encoding a ligand that binds to a substrate present on the surface of a cell.

[2. The chimeric pIX protein of claim 1, wherein the non-native amino acid sequence is a ligand or an antigen.]

[3. The chimeric pIX protein of claim 2, wherein the non-native amino acid sequence is a ligand that binds to a substrate present on the surface of a cell.]

4. (Amended) The chimeric pIX protein of claim [3] 1, wherein the ligand recognizes a CD40 [antigen] protein.

5. (Amended) The chimeric pIX protein of claim [3] 1, wherein the ligand is an RGD-containing or polylysine-containing sequence.

19. (Amended) An adenoviral capsid containing [the] a chimeric pIX protein having at least one adenoviral pIX domain and a non-native amino acid sequence [of claim 1].

41. (New) A chimeric pIX protein having at least one adenoviral pIX domain and a non-native amino acid sequence encoding an antigen, wherein the non-native amino acid sequence constitutes the C-terminus of the chimeric pIX protein or is located internally within the chimeric pIX protein.

42. (New) The chimeric pIX protein of claim 41, wherein at least one adenoviral pIX domain consists essentially of an adenoviral pIX peptide sequence truncated at the C-terminus.

43. (New) The chimeric pIX protein of claim 41, wherein at least one adenoviral pIX domain consists essentially of an adenoviral pIX peptide sequence truncated at the N-terminus.

44. (New) The chimeric pIX protein of claim 41, comprising a first adenoviral pIX domain consisting essentially of an adenoviral pIX peptide sequence truncated at the C-terminus and a second adenoviral pIX domain consisting essentially of an adenoviral pIX peptide sequence truncated at the N-terminus.

45. (New) The chimeric pIX protein of claim 44, wherein the first and the second adenoviral pIX domains do not share any common peptide sequences.

46. (New) The chimeric pIX protein of claim 44, wherein a spacer peptide domain separates the first and the second adenoviral pIX domains.

47. (New) The chimeric pIX protein of claim 41, having an adenoviral pIX domain consisting essentially of a full-length adenoviral pIX peptide sequence.

48. (New) A nucleic acid encoding the chimeric pIX protein of claim 41.

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For: ADENOVIRAL CAPSIDS CONTAINING CHIMERIC PROTEIN IX

PENDING CLAIMS AFTER AMENDMENTS MADE IN RESPONSE TO OFFICE ACTION DATED JANUARY 3, 2002

1. A chimeric pIX protein having at least one adenoviral pIX domain and a non-native amino acid sequence encoding a ligand that binds to a substrate present on the surface of a cell.

4. The chimeric pIX protein of claim 1, wherein the ligand recognizes a CD40 protein.

5. The chimeric pIX protein of claim 1, wherein the ligand is an RGD-containing or polylysine-containing sequence.

6. The chimeric pIX protein of claim 1, wherein the non-native amino acid is constrained by a peptide loop within the chimeric protein.

7. The chimeric pIX protein of claim 6, wherein the loop comprises a disulfide bond between non-adjacent amino acids of the protein.

8. The chimeric pIX protein of claim 1, wherein the non-native amino acid sequence constitutes the C-terminus of the chimeric protein.

9. The chimeric pIX protein of claim 1, wherein the non-native amino acid sequence constitutes the N-terminus of the chimeric protein.

10. The chimeric pIX protein of claim 1, wherein the non-native amino acid sequence is located internally within the chimeric protein.

11. The chimeric pIX protein of claim 1, wherein at least one adenoviral pIX domain consists essentially of an adenoviral pIX peptide sequence truncated at the C-terminus.

12. The chimeric pIX protein of claim 1, wherein at least one adenoviral pIX domain consists essentially of an adenoviral pIX peptide sequence truncated at the N-terminus.

13. The chimeric pIX protein of claim 1, comprising a first adenoviral pIX domain consisting essentially of an adenoviral pIX peptide sequence truncated at the C-terminus and a second adenoviral pIX domain consisting essentially of an adenoviral pIX peptide sequence truncated at the N-terminus.

14. The chimeric pIX protein of claim 13, wherein the first and the second adenoviral pIX domains do not share any common peptide sequences.

15. The chimeric pIX protein of claim 13, wherein a spacer peptide domain separates the first and the second adenoviral pIX domains.

16. The chimeric pIX protein of claim 15, wherein the spacer peptide domain comprises the ligand domain.

17. The chimeric pIX protein of claim 1, having only one adenoviral pIX domain consisting essentially of a full-length adenoviral pIX peptide sequence.

18. A nucleic acid encoding the chimeric pIX protein of claim 1.

19. An adenoviral capsid containing a chimeric pIX protein having at least one adenoviral pIX domain and a non-native amino acid sequence.

20. The adenoviral capsid of claim 19, which binds dendritic cells.

21. The adenoviral capsid of claim 19, comprising a mutant adenoviral fiber protein having an affinity for a native adenoviral cellular receptor of at least about an order of magnitude less than a wild-type adenoviral fiber protein.

22. The adenoviral capsid of claim 19, comprising an adenoviral penton base protein having a mutation affecting at least one native RGD sequence.

23. The adenoviral capsid of claim 19, comprising an adenoviral hexon protein having a mutation affecting at least one native HVR sequence.

24. The adenoviral capsid of claim 19, lacking a native glycosylation or phosphorylation site.

25. The adenoviral capsid of claim 19, which is conjugated to polyethylene glycol.

26. The adenoviral capsid of claim 19, which elicits less immunogenicity in a host animal than does a wild-type adenovirus.

27. The adenoviral capsid of claim 19, comprising a second non-adenoviral ligand conjugated to a fiber, a penton, a hexon, a protein IIIa or a protein VI.

28. The adenoviral capsid of claim 27, wherein the non-native amino acid is a ligand and wherein the second non-adenoviral ligand recognizes the same substrate as the non-native amino acid.

29. A composition of matter comprising the adenoviral capsid of claim 19 and a nucleic acid.

30. The composition of matter of claim 29, further comprising a liposome.

31. An adenoviral vector comprising the adenoviral capsid of claim 19 and an adenoviral genome.

32. The adenoviral vector of claim 31, which is replication incompetent.

33. The adenoviral vector of claim 31, which does not productively infect HEK-293 cells.

34. The adenoviral vector of claim 31, wherein the adenoviral genome comprises a non-native nucleic acid for transcription.

35. The adenoviral vector of claim 34, wherein the non-native nucleic acid for transcription is operably linked to a non-adenoviral promoter.

36. The adenoviral vector of claim 35, having a ligand that binds to a substrate present on the surface of a cell and wherein the non-adenoviral promoter is active within the cell.

37. The adenoviral vector of claim 35, wherein the non-adenoviral promoter is a tissue-specific promoter.

38. The adenoviral vector of claim 35, wherein the non-adenoviral promoter is a regulable promoter.

39. A method of infecting a cell, comprising contacting a cell with an adenoviral vector of claim 31.

40. The method of claim 39, wherein the adenoviral genome comprises a non-native nucleic acid encoding a protein, and wherein the nucleic acid is expressed within the cell to produce the protein.

41. A chimeric pIX protein having at least one adenoviral pIX domain and a non-native amino acid sequence encoding an antigen, wherein the non-native amino acid sequence constitutes the C-terminus of the chimeric pIX protein or is located internally within the chimeric pIX protein.

42. The chimeric pIX protein of claim 41, wherein at least one adenoviral pIX domain consists essentially of an adenoviral pIX peptide sequence truncated at the C-terminus.

43. The chimeric pIX protein of claim 41, wherein at least one adenoviral pIX domain consists essentially of an adenoviral pIX peptide sequence truncated at the N-terminus.

44. The chimeric pIX protein of claim 41, comprising a first adenoviral pIX domain consisting essentially of an adenoviral pIX peptide sequence truncated at the C-terminus and a second adenoviral pIX domain consisting essentially of an adenoviral pIX peptide sequence truncated at the N-terminus.

45. The chimeric pIX protein of claim 44, wherein the first and the second adenoviral pIX domains do not share any common peptide sequences.

46. The chimeric pIX protein of claim 44, wherein a spacer peptide domain separates the first and the second adenoviral pIX domains.

47. The chimeric pIX protein of claim 41, having only one adenoviral pIX domain consisting essentially of a full-length adenoviral pIX peptide sequence.

48. A nucleic acid encoding the chimeric pIX protein of claim 41.